Special Medical Augmentation Response Team

Veterinary

(SMART-V)

The end of the Cold War signaled the emergence of a "New World Order;" unfortunately, reality has proven that this "New World Order" is neither new nor orderly. Until very recently, Americans felt secure in the fact that terrorism occurred only outside of U.S. borders. However, within the last five years, 11 states have experienced acts of terrorism. Additionally, worldwide environmental and man-made catastrophes have heightened U.S. public concern of the associated humanitarian needs with these situations. Finally, natural disasters have the potential to affect large populated areas and cause severe destruction.

Animals may be affected by these same types of catastrophes, or may be brought into the area as rescue animals. In the event of biological warfare, many potential agents are also pathogenic to animals. For all these reasons, Veterinarians must be an integral part of any assessment or response plans. The Army Medical Command has formed 8 types of teams, one of them a veterinary team, to rapidly respond to a natural or man-made disaster, deploy to the affected area, assess the incident and recommend what assets are required to resolve the incident. These teams are meant to augment local military or civilian first responders, not replace them.

The SMART-V team's mission is to assess the degree of existing destruction and/or impending risk and to determine recommended follow-on actions relative to animal health and food safety. The SMART-V teams have the capability to rapidly deploy a full complement of veterinary food and animal care experts. Their main focus will be to assess the incident and recommend follow-on support. Communication with federal and civilian veterinary organizations is the key, with the ultimate goal of a coordinated effort between civilian, state and federal veterinary organizations to resolve the incident.

SMART-V personnel consist of:

Commander, Preventive Medicine Veterinarian (ACVPM)

Preventive Medicine Veterinarian (ACVPM)

Food Inspection Warrant Officer (BS/MS)

Clinical Medicine Veterinarian (ACVIM, ACVS, other)

Senior Animal Care Technician (LVT/RVT)

Laboratory Animal Veterinarian (ACLAM)

SMART-V capabilities include:

a. Assistance to civil authorities in determining follow-on specialty skills and medical resources

required to resolve the incident relative to animal health and food safety.

b. Technical expertise in veterinary preventative medicine issues to include foodborne illness risk/outbreaks and zoonotic disease risk/outbreaks.

c. Coordination of veterinary care for military search and rescue dogs; when authorized, it also coordinates care to other governmental and nongovernmental agencies' animals participating in the operation.

d. Limited triage and emergency medical care using on-scene facilities/resources and backpack/hand carried trauma kits. When appropriate, provides euthanasia to prevent undue suffering of those cases encountered during the assessment process.

e. Technical expertise in animal triage, trauma management, evacuation, confinement, euthanasia, and carcass disposal.

f. Assisting authorities in developing a transition plan which facilitates an orderly return to pre-incident operations.

United States Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services

Early Response Team (ERT)

To assist local jurisdiction in making a diagnosis while assessing and advising the governing body of the risks of an epidemic or negative impact of an animal disease outbreak, the rapid collection of data and its evaluation by the ERT would be a basis to quickly decide to activate part or all of the jurisdictions emergency response system to manage the health event. Critical components of their investigations include identifying and characterizing the etiologic agent, describing the illness, determining the modes and vehicles of transmission, and begin developing immediate and longer-term prevention strategies.

The purpose of the ERT is defined as assisting the local FAD (foreign animal disease) diagnostician in making a diagnosis while assessing and advising the agency of the risks of an epidemic or an FAD. The rapid collection of data and its evaluation by the ERT would be a basis to quickly decide to activate part or all of the READEO (Regional Emergency Animal Disease Eradication Organization) to manage the health event.

Member of the team include: a pathologist, epidemiologist, diagnostician, local FAD diagnostician (FADD), and a local State or tribal field veterinarian/livestock inspector. The local FADD and the state official must be available as much as possible during the team's visit. The state/tribal person is important as a resource person for the team and as a point person for the State Veterinarian or Tribal Officials.

Criteria for Deployment: a visit to the site of the health event and assessment by a FADD. It is highly desirable that a written assessment be sent to ERT members through the READEO director before deployment. Evidence of spread to or involvement of several premises or groups of animals. Or, high potential of spread to multiple premises bases on the laboratory-confirmed diagnosis of a highly communicable disease. The concurrence of the State Veterinarian/ Tribal Officials, AVIC, Regional Director, and READEO Director.

The ERT members are highly specialized and are available on immediate notice. They are also busy with many responsibilities at their home station. The best use of the ERT members is for short-term diagnostic assistance and rapid assessment of unusual disease syndromes, and not for longer-term management of a health program. For further assistance or diagnostic work, the ERT can decide the amount of time needed or required. The assessment will include the differential diagnosis, case definition, risk of an FAD, the risk of spread, pathogenesis, expected duration, means of transmission, morbidity, mortality, effectiveness of control measures, and other factors that might be important in determining the scope of a potential READEO deployment.

OVERVIEW OF A DISASTER OPERATION

This overview illustrates response and recovery actions Federal agencies likely will take to help State and local governments that are overwhelmed by a major disaster or emergency. Key operational components that could be activated include the Regional Operations Center (ROC), Emergency Response Team — Advance Element (ERT-A), National Emergency Response Team (ERT-N), Emergency Support Team (EST), Emergency Response Team (ERT), Disaster Field Office (DFO), Catastrophic Disaster Response Group (CDRG), and Disaster Recovery Center (DRC).

1. FEMA's National Emergency Coordination Center continually monitors potential disasters and emergencies. When advance warning is possible, FEMA may deploy, and may direct Federal agencies to deploy liaison officers and personnel to a State Emergency Operations Center to assess the emerging situation. A ROC may be activated, fully or partially. Facilities, such as mobilization centers, may be established to accommodate personnel, equipment, and supplies.

2. Immediately after a disaster, local jurisdictions respond using available resources and notify State response elements. As information emerges, they also assess the situation and request State assistance if needed. The State reviews the situation, mobilizes State resources, and informs the FEMA Regional Office of actions taken. The Governor declares a state of emergency, activates the State emergency operations plan, and requests a Presidential disaster declaration. The State and FEMA jointly conduct a Preliminary Damage Assessment to validate the State's request and determine the kind of Federal assistance needed.

3. After the declaration, a ROC, staffed by regional personnel, coordinates initial regional and field activities such as deployment of an ERT-A. The ERT-A assesses the impact of the event, gauges immediate State needs, and makes preliminary arrangements to set up operational field facilities. (If regional resources appear to be overwhelmed or if the event has potentially significant consequences, FEMA may deploy an ERT-N.)

4. An interagency EST, composed of Emergency Support Function (ESF) representatives and FEMA support staff, carries out initial activation and mission assignment operations and supports the ROC from FEMA Headquarters.

5. A Federal Coordinating Officer (FCO), appointed by the FEMA Director on behalf of the President, coordinates Federal activities. The FCO works with the State Coordinating Officer to identify requirements.

6. The FCO heads the interagency ERT. The ERT works with the affected State and conducts field operations from the DFO. ESF primary agencies assess the situation and identify requirements. Under FEMA mission assignments or their own authorities, agencies supply goods and services to help the State respond effectively.

7. The CDRG, composed of representatives from FRP signatory agencies, convenes at FEMA Headquarters when needed to provide guidance and policy direction on coordination and operational issues. The EST supports the CDRG and coordinates with the ERT.

8. As immediate response priorities are met, recovery activities begin in the field. Federal and State agencies helping with recovery and mitigation convene to discuss State needs.

9. Teleregistration is activated and has a toll-free telephone number disaster victims can call to apply for assistance. A toll-free disaster helpline is established to answer common questions. One or more DRCs may be opened where victims can obtain information about disaster assistance, advice, and counsel. The affected area is inspected to determine the extent of damage, and funds for approved assistance are obligated.

10. Concurrently, Applicant Briefings are conducted for local government officials and certain private nonprofit organizations to inform them of available assistance and how to apply. Applicants must first file a Request for Public Assistance. Eligible applicants will then be notified and will define each project on a

Project Worksheet, which details the scope of damage and a cost estimate for repair to a pre-disaster condition. The Project Worksheet will be used as the basis for obligating funds to the State for eligible projects.

11. Throughout response and recovery, mitigation staff at the DFO examines ways to maximize mitigation measures. Hazard Mitigation Site Survey Teams contact local officials to identify potential projects and suggest which ones should be included in an early implementation strategy. The strategy, produced in cooperation with Federal, State, and local officials, focuses on viable opportunities to provide funds, technical assistance, and staff support to incorporate mitigation into the repair and replacement of damaged or destroyed housing and infrastructure.

12. As the need for full-time interagency coordination at the DFO ceases, the ERT plans for selective release of Federal resources, demobilization, and closeout. Federal agencies then work directly with their grantees from their regional or headquarters offices to administer and monitor individual recovery programs, support, and technical services.

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Rift Valley Fever: A Zoonotic Disease

Introduction (Slide #1 Title)?

The disease I will be discussing only periodically receives notoriety and, unless you live and work in endemic areas, Rift Valley fever may not be familiar to you.

Overview (Slide #2 RVF Definition)

Rift Valley fever is a viral zoonosis that may cause severe disease in both animals and humans. Rift Valley fever virus is a member of the *Phlebovirus* genus in the family *Bunyaviridae*. The virus is transmitted primarily by the bite of infected mosquitoes.

(Slide #3 Grassland habitat) The virus is typically associated with pastoral regions where habitat conducive to the maintenance of arthropod vectors is present. Natural hosts for RVF virus include mosquitoes, ruminants, and humans. Newborn lambs and calves are highly susceptible. The disease produces high animal morbidity and mortality causing a substantial economic hardship due to losses in livestock and livestock production. **(Slide #4 History)** Since the first isolation of the virus and a detailed description of the disease in sheep in the Rift Valley of Kenya in 1931 there have been significant epizootics in Kenya, South Africa where the first human deaths were recognized in the 1975 outbreak, Egypt in 1977 and 1993, and West Africa in 1987. Heavy rainfall throughout eastern Africa contributed to a major outbreak in Kenya and Somalia in 1997-98, and the most recent outbreak occurred in Mauritania in 1998. **(Slide #5 Africa map)** Presently, virologic and serologic evidence suggests that the virus exists throughout sub-Saharan Africa and Madagascar and, in light of its recurrence in Egypt in 1993, may be extending its range even further, although, to date, no outbreaks have been reported outside Africa. Modern transportation provides a potential means for global transmission via infected animals and humans incubating the virus as well as infected vectors carried as stowaways. Hence, international travelers to endemic areas should be aware of the disease and its public health and agricultural importance.

The Virus (Slide #6 Natural Cycle)

In the absence of epidemics, a cycle of enzootic circulation exists in many regions of Africa. Livestock infections, probably acquired by the bite of infected mosquitoes, result in low rates of disease and abortion that are undiagnosed due to confusion with other livestock diseases as well as a lack of diagnostic

capabilities. Reservoirs for RVF virus are unidentified, though there is strong evidence of interepidemic maintenance via transovarial transmission in certain *Aedes* mosquitoes. The infected eggs are deposited and may remain dormant in depressions, called "dambos" in East Africa or "pans" in South Africa, that are subject to inundation. When flooding occurs, the eggs hatch and infected larvae emerge and develop into infected adults. Through monitoring of changes in vegetation, satellite remote sensing is being used to identify those areas of flooding that may trigger hatching of floodwater *Aedes* and provide breeding sites for secondary vectors.

(Slide #7 Cow) Epidemics of RVF typically center around regions where there are large concentrations of sheep and cattle. Explosive epidemics occur periodically and are usually associated with periods of heavy rainfall producing localized flooding and dense or expanding vector populations. **(Slide #8 Epizootic Cycle)** Transovarially infected floodwater *Aedes* eggs hatch producing infected adults that feed extensively on cattle. Other mosquito species feeding on infected livestock ingest viremic blood meals and, if those mosquitoes are efficient vectors, develop disseminated infections and become competent secondary vectors. Viremic blood is also a source of infection at slaughter and necropsy. **(Slide #9 Transmission)** Secondary vectors include mosquitoes of many species of the genera *Anopheles, Culex, Eretmapodites, and Mansonia. Culicoides* spp. and sand flies may play limited roles in biological transmission and, along with other arthropods, mechanical transmission. *Culex pipiens* was an important mosquito vector in the Egyptian epizootic in 1977.

Although aerosol transmission between infected and susceptible livestock appears less important than mosquito transmission, humans may be infected by aerosol in the laboratory and during slaughter of viremic animals. Blood, serum, and the products of abortion from RVF virus-infected animals are sources for infection of humans in at-risk occupations such as abattoir workers, farmers, veterinarians, and laboratory technicians. Consumption of milk or meat from infected animals does not appear to be a common means of transmission.

High concentrations of virus may be found in amniotic fluid and the serosanguinous fluid in the thorax of aborted lamb carcasses and may provide a source of environmental contamination as well as diagnostic material.

CLINICAL FEATURES

In Africa, the disease in animals seems to be limited to domestic ruminants, with imported European animals being more severely affected than native African breeds. Sheep and cattle are the primary domestic ruminant species affected by RVF virus, with goats being involved to a lesser extent.

(Slide #10 Peracute Signs) Clinical signs vary considerably and are related to the species and age of the animal involved. Disease progression and severity of disease are generally inversely proportional to age. Adult cattle and sheep may suffer mortality rates of 10-30% or higher, depending on the nutritional state of the animal; but in animals fewer than 7 days old, fatality rates may approach 100%. The disease is characterized by a short incubation period, fever often exceeding 42C, hepatitis, abortion, and death. **(Slide #11 Fetuses)** Widespread abortion, infertility and rapidly fatal neonatal disease are typical of outbreaks among cattle and sheep. Fulminant neonatal disease may be the first indication of RVF in areas where abortion rates are high due to other abortogenic agents. **(Slide #12 Clinical Signs)** Other overt signs are inconsistent, but include congestion of mucous membranes, mucopurulent nasal discharge, vomiting, anorexia, general weakness, an unsteady gait, fetid diarrhea, and a rapid decrease in milk production. A definite leukopenia, most severe in younger animals, which corresponds to maximal viremia and temperature response, is seen, often followed by leukocytosis in later stages of the disease. Elevated liver function test values are common. Experimentally infected animals are viremic for 2 to 5 days with titers often in excess of 10^8 plaque-forming units per ml (PFU/ml). No long-term carrier state in animals has been identified. Central nervous system involvement, evidenced by encephalitis, occurs periodically in experimentally infected rodents surviving a week or more after experiencing a brief episode of low viremia or in animals with high viremias that have been treated with antiviral drugs or passive antibodies. While, the incidence of encephalitis in cattle naturally infected with RVF virus is not known, there is a single report of RVF viral encephalomyelitis in an experimentally infected calf.

(Slide #13 Human Disease) The disease in humans is usually a temporarily incapacitating illness. The incubation period may vary from two to six days. There then follows a dengue-like illness, with a sudden onset of fever, malaise, headache, myalgia, and backache. Some patients also develop neck stiffness, photophobia, and vomiting followed by complete recovery. The symptoms of RVF usually last for about one week. Probably 1% or less of human infections progress to the more severe and often fatal complications of hemorrhagic disease, encephalitis, or retinal disease. The determinants of these different syndromes are unknown. However, during the RVF virus outbreak in Egypt in 1993, a presumptive case definition of ocular disease characterized by macular and paramacular retinal lesions, frequently with hemorrhage and edema, following a febrile episode was established. **(Slide #14 Egyptians)** This clinical presentation was quite different from the previous outbreak in 1977-1978 in which the hemorrhagic form was frequently seen and accounted for nearly 600 human deaths.**(Slide #15 Abdominal Rash)** Animal losses due to abortion and mortality

were high and impacted significantly on the availability and cost of animal protein in Egypt.

The introduction of RVF virus into Egypt in 1977 produced the largest recorded RVF epidemic. Before this epidemic, only four human deaths attributable to RVF had been reported. The sudden and unexpected appearance of this previously geographically limited sub-Saharan virus and the unprecedented numbers of encephalitic, ocular, and fatal hemorrhagic disease remains an enigma. Introduction by means of importation of diseased animals from the south or wind-borne arthropods are unproven possibilities. The epidemic centered in the fertile Nile Delta region harboring an essentially naive population of human, livestock, and arthropod hosts and vectors. The demography of the region coupled with an alteration in virulence of the virus, perhaps through reassortment, and the presence of endemic hepatotropic diseases, like *Schistosoma mansoni*, may have contributed to this devastating epizootic.

The presence of serum antibody to RVF virus seems to be the major immunological defense mechanism in recovery. Under experimental conditions, the outcome of RVF virus infection appears to be regulated by serum antibody and interferon, and the early appearance of serum interferon may be a contributory factor in limiting viremia and preventing clinical disease.

PATHOLOGIC FEATURES (Slide #16 Gross Pathology)

The most consistent pathologic changes in all species affected involve the liver. The liver appears to be the primary site of virus replication and initial mild hepatocellular changes rapidly progress to final massive necrosis. As the disease progresses in neonates, the necrotic foci may enlarge to 2 mm in diameter and the liver becomes friable, irregularly congested, and may become mottled brown or yellow. **(Slide #17 Liver)** As these necrotic areas enlarge, extensive destruction of normal hepatic architecture occurs. Hepatic lesions in adult ruminants are not as severe as those found in neonates, but multiple necrotic areas may be present. In some animals only small, microscopic necrotic areas with varying degrees of visceral and serosal hemorrhages are seen. Coagulated blood may be found in the lumen of the gallbladder in those cases with marked hemorrhage in the liver. Hemorrhages are seen infrequently in the abomasum and intestinal tract. **(Slide #18 Placenta)**

DIAGNOSIS and TREATMENT (Slide #19 Diagnosis)

An epidemiological pattern suggestive of RVF includes short incubation period; high mortality in lambs, calves, and kids that are less than 1 week old; illness in adult sheep and cattle; high abortion rates among cows and ewes; liver lesions at necropsy; an acute febrile disease in humans; and the presence of dense populations of arthropod vectors. **(Slide #20 Differential Dx)**

(Slide #21 Microscopic Path) In the laboratory, a characteristic histopathological finding of liver necrosis in all susceptible animals often provides the first clue that the disease is RVF. **(Slide #22 H&E Liver)** Microscopically, extensive moderate to severe centrolobular and midzonal coagulative necrosis occurs in all lobes of the liver. A definitive diagnosis of RVF is accomplished by isolating and identifying the virus or by observing a fourfold rise in specific, neutralizing antibody titer between acute and convalescent sera. **(Slide #23 Samples)** During past epizootics, the most common material used for virus isolation included whole blood or serum collected from animals at the peak of pyrexia. Fresh specimens of liver from animals dying of the illness and the products of abortion are also excellent diagnostic materials. Infected humans are also a source of diagnostic material; and, if possible, suspected mosquito vectors should be collected for virus-isolation studies.

(Slide #24 Virologic Dx) RVF virus may be isolated in laboratory rodents as well as in a number of common cell culture systems; however, virus isolation should not be attempted unless adequate personal protection, such as vaccination, can be assured or biosafety level 3 (BSL-3) containment facilities are available. Laboratory animals of choice for isolation are suckling mice, adult mice, and hamsters. RVF virus is one of the few viruses that will kill adult mice and hamsters within 1 to 4 days after intraperitoneal inoculation.

(Slide #25 Serologic Dx) Serological techniques used to demonstrate RVF virus antibody in domestic animals and humans include HI, CF, IFA, agar gel diffusion, plaque-reduction neutralization, and ELISA tests. The ELISA is also used to demonstrate viral antigen in suspect tissue and serum. Nucleic acid hybridization and enzyme immunochemistry techniques for detection of viral antigen have been useful but are less sensitive than virus isolation. Polymerase chain reaction (PCR) methodology is exquisitely sensitive and specific and its utility as a diagnostic tool for RVF virus is being evaluated.

TREATMENT AND CONTROL (Slide #26 Control)

No specific treatments are currently available. RVF virus is sensitive to several antiviral agents and interferon in vitro. Experimental studies show that ribavirin and recombinant interferon alpha are effective prophylactic drugs; however, chemotherapeutic efficacy for the disease has not been demonstrated. Passive antibody therapy, by administration of immune plasma or serum, may be effective but impractical in an epizootic. Neonatal calves have been shown to be completely protected against experimental challenge with virulent virus through ingestion of colostrum from immune dams.

Relocating animals to an altitude where mosquitoes are absent or applying residual insecticides to animals and their pens and barns has been suggested, though movement of animals

during an epizootic is undesirable and rarely practical, and effectiveness of residual insecticides in animal-holding areas depends on vector habits. Limiting amplification of virus in domestic animals will probably block extensive human disease and mass vaccination is the method of choice in controlling RVF during an epizootic.

Effective live-attenuated and killed veterinary vaccines for RVF are in use in many African countries. The live-attenuated Smithburn strain provides long-lasting immunity but is abortogenic in pregnant ewes. The live-virus vaccines should be used only in enzootic areas of Africa or to control an epizootic.

Killed vaccines are recommended for use outside enzootic areas of Africa. A formalin-inactivated vaccine is safe for pregnant ewes but provides only short-term immunity and requires booster inoculations to maintain a durable immunity. Stringent production controls are necessary to ensure the absence of residual live virus.

The only vaccine cleared for human use is a killed product available only from the United States Army Medical Research and Materiel Command (USAMRMC). This vaccine is in limited supply and requires an initial three-dose series for protective immunity with annual booster inoculations required to maintain that immunity.

A live, attenuated vaccine (MP-12) developed for use in livestock and humans is being tested. Extensive laboratory studies have shown this vaccine to be safe and efficacious against virulent virus challenge in pregnant cows and ewes as well as in neonatal calves and lambs. Under experimental conditions, the vaccine does not induce fetal damage in sheep or cattle. Limited field studies in Senegal have shown the MP-12 vaccine to be safe, immunogenic, and nonabortigenic. The MP-12 vaccine is less neurovirulent than the Smithburn strain in rhesus monkeys and, because the genome of this virus has at least one attenuating lesion on each of the three segments, reversion to virulence is unlikely, and reassortment with wild-type virus would produce attenuated progeny.

Suggested specific measures to control a Rift Valley fever epidemic include:

1. Implement an animal vaccination program by using a live, attenuated RVF vaccine (inactivated vaccine for pregnant animals and neonatal lambs).

a. Establish a vaccine barrier between known affected areas and unaffected areas.

b. Positively identify vaccinated animals with an ear tag, tattoo, or other means of identification not easily counterfeited or duplicated.

c. Prohibit the use of common needles to immunize herds or flocks.

d. Prohibit the movement of non-vaccinated animals from affected areas.

e. Employ integrated vector control measures in the areas of active virus transmission and elsewhere as practical and appropriate. Use caution when using insecticides to prevent destruction of mosquito predator species as well as contamination of water and food supplies.

f. Use personal protective measures such as insect sprays, repellents, and bednets.

2. Implement active surveillance for human and animal disease as well as seroprevalence outside the area of active virus transmission.

a. Inform human health care providers and veterinarians of the present epizootic/epidemic and be alert for cases exhibiting common signs and sequelae of the disease.

b. Alert those in high-risk occupations (farmers, herdsmen, and abattoir workers) to the potential hazard of aerosol and parenteral infection through the slaughtering of sick animals and assisting with abortions or handling of products of abortion from ruminants.

c. Increase public awareness of the threat through radio, newspaper, and television broadcasts and instructions in personal protective measures. This information should be truthful, accurate, and informative, and care must be taken to instruct and not induce panic or over-reaction.

3. Vaccination should be sought for abattoir workers and certain professionals such as veterinarians, physicians, health care providers, biomedical researchers, and laboratory technicians who are at greatest risk of infection through their attendance to patients or processing of laboratory specimens.

CONTROL AND PREVENTION OF A NOVEL VIRAL PATHOGEN

Week 1

Background:

On August 20, 1999 you are contacted by the Health Department from State A (More information on the geography, attachment 1) requesting assistance with a perceived public health problem. Physicians there have seen substantial increases in the number of people admitted to the areas hospitals with encephalitis. People are presenting with a cough, fever and headache and within a couple of days about 50% develop neurologic sequella and require supportive care. Thus far physicians have not been able to determine the cause of the illness but have identified a new virus from one of the patients, the virus is from the family Paramyxoviridae. (More information on the virus, attachment 2) The new virus is similar to Hendra virus discovered in Australia in 1994. Hendra is considered a BSL- 4 agent (More information on BSL criteria, attachment 3). At this time, 244 people have fallen ill and of those 44 are on respirators and four have died. Additionally patients continue to come in daily (Attachment 4).

Physicians noted that most of the victims are associated with pig farming in one way or another. Of the patients thus far 31 patients are from Area Z and the rest from Area X (More information on the geography and pig farming, attachment 1).

There are approximately 200,000 pigs in area 1; 300,000 in area 2; 400,000 in area 3; 250,000 in area 4; with the remaining pig population in 6 & 7. Slaughter houses are generally located in each pig production area. Pigs are moved via trucks to markets both within State A and out to C & B States.

Objectives:

1. Determine if there are "really" increases in human and animal disease above normal, and if there is a connection between the human cases and pig farming.(How you would establish disease trends in pigs and where you would find this information for both humans and pigs.
2. Identify the role "if any" that pigs play, and "how" you would establish this association
    a. Identify assets needed, expertise as well as equipment
    b. Determine an estimated time line, how long will it take for your team to get in the field, set up a laboratory, identify clinical patterners and implement control methods
        i. Identify risk groups
        ii. Develop preventive measures
    c. What additional information would you like that "may" be available from local healthcare professionals and agriculture specialists? (More information on the swine disease, attachments 5 and 6)
3. Are there any immediate public heath recommendations you would like to implement at this time?

Assumptions: Your field team cannot exceed 15 members and must investigate the human illness as well as animal. You have access to a state-of-the-art laboratory but there are no local laboratory personnel available to assist with this investigation. The initial identification of this virus was done by a reference lab but they are not capable of continuing support. Your job is to investigate the outbreak for both human and animal perspectives and make appropriate recommendations to alleviate human disease and possibly maintain a viable livestock industry. The State Department of Agriculture is willing to help but have other priorities and this has limited the manpower they can dedicate to helping your group. Only Pig Farming Area 1 and 2 have reported sick pigs.

CONTROL AND PREVENTION OF A NOVEL VIRAL PATHOGEN

Week 2

Background:

Over the last 8, days 48 new human cases have been admitted to the hospital and there have been an additional 25 deaths. Laboratory tests have indicated that the same virus is responsible for disease in humans and pigs. All but two of the new cases are associated with pigs and have come from Areas Z and X. State A has developed a "Task Force" and declared a "State of Emergency". Some farmers are fleeing their farms, out of fear for their lives. This has resulted in many pigs starving to death or escaping from the farms. This is the second week of the epidemic and consumption of pork has ceased. National attention has been focused on State A and all other states have stopped receiving all animal products at this time.

State and local veterinarians along with pig farmers have developed a case definition with your help (Updated case definition, attachment 7). There are many farmers reporting pigs with disease and some farmers and state veterinarians have indicated that other domestic animals may be sick as well. Species listed as being ill are dogs, cats, rats, horses, goats, chickens and ostriches. Pig Farming Areas 1 and 2 are considered to be completely infected. The only new area to report disease in pigs is from Area 4 and this has been verified but there have not been any human cases reported.

Laboratory personnel have developed an ELISA test for both IgM and IgG for pigs, dogs and cats. Information on the lab test is available (See attachment 8).

Objectives:

1. If you have not already done so, develop, a National Control and Surveillance program for swine.
    a. Identify assets needed, labor necessary to implement the program and possible sources of labor.
    b. Determine short and long term program elements and provide a time estimate for bringing the epidemic under control and reestablishing the swine production in State A.
        i. Establish a swine testing protocol that would identify previously infected pig farms and newly infected farms
    c. Discuss possible methods for depopulation of swine infected with a BSL 4 pathogen
        i. Determine personal protective equipment needed
        ii. Number of personnel needed to depopulate 1million pigs and time necessary to complete this undertaking
2. What are the immediate public heath recommendations you would like to implement at this time?

Assumptions: Your laboratory is up and running and turn around time for specimens is approximately 4 days. You have established that people are being infected by contact with diseased pigs. You have all the assets of State A at your disposal at this time. You must develop a National Control and Surveillance Program based on available information to minimize human infection and stop this epidemic. You don't know how the virus got into the pigs but it is obvious that the movement of sick pigs is responsible for spreading the disease within State A.

When farms become infected approximately 90% of the adult animals sero-convert with 50% of the animals less than 7 months showing signs of illness. Mortality in all age groups of swine is between 1-5 %.

Attachment 1

Geography:

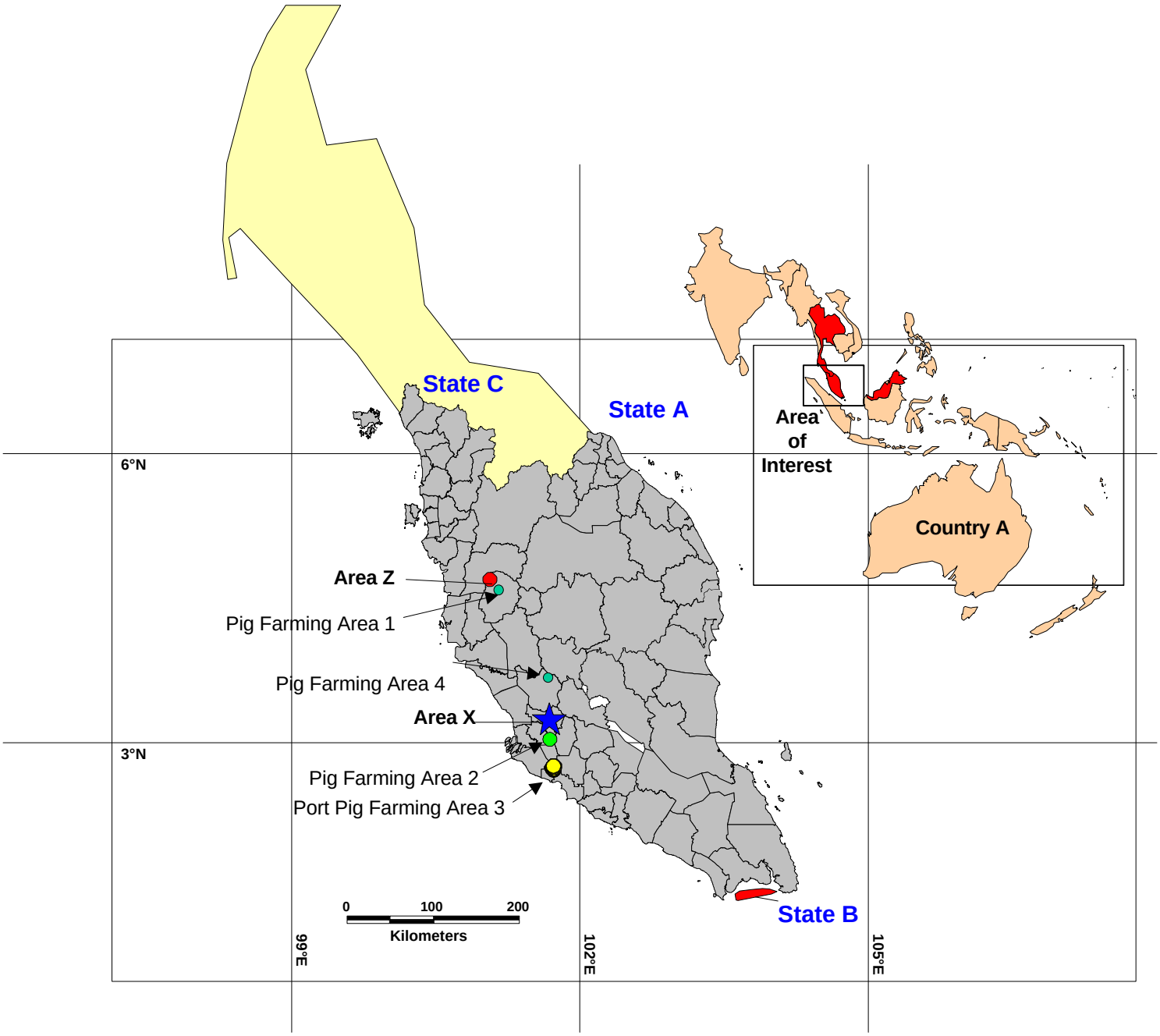
The area for this exercise is sub-tropical, with the average rainfall per year of approximately 100 inches. The wet season is from October to April. The average temperature is ~80°F. There are two population centers with two-million in the capital of State A and another million in north, City B. Area X has approximately 250,000 people within the dashed area while Area Z has 100,000. Total human population for the entire State is 5 million. (See map)

Pig Farming:

Pig farming in State A is primary commercial with ~2.5 million standing pig population. Pigs farms are generally located within seven distinct areas, (1-7). Within the pig farming areas the majority of the farms are located within .5 kilometer of each other. This was done to decrease operational costs, similar to the bovine feedlot operations within the United States. Pigs are sold to both in-state and out-of-state slaughter houses. Pigs are raised to approximately six-seven months prior to slaughter. Farms average about 1000 head with a few farms maintaining as many as 30,000 head. In State A, pig farming accounts for 5% of the states income.

Communities have developed around the pig farming regions and generally provide all the necessary equipment, feed and care for that farming community. On the average 20,000 people live in a pig farming community and come in direct contact with the pigs. Most farms have quarters for the farm laborers on the premises.

Breeding stock are brought in from other states or by trading between farms. When pigs are shipped they are picked up at each farm until the trucking company has a full load and then transported to the slaughter house.


State C
State A
Area of Interest
Country A
Area Z
Pig Farming Area 1
Pig Farming Area 4
Area X
Pig Farming Area 2
Port Pig Farming Area 3
State B
6°N
3°N
99°E
102°E
105°E
0
100
200
Kilometers

Attachment 2

OVERVIEW OF PARAMYXOVIRUSES

The family Paramyxoviridae comprises a large number of viruses that cause both human and animal disease. Paramyxoviruses are negative-stranded, pleomorphic enveloped RNA viruses that generally exhibit specificity over a single or limited host range. Although these viruses have previously been classified by serology, current classification is based on nucleotide sequencing and other genomic structural characteristics. There are two major groupings within the family, the subfamily containing the pneumoviruses and the subfamily containing the other paramyxoviruses. Within the subfamily paramyxovirinae, four main subgroups are the parainfluenza viruses, the rubalaviruses morbilliviruses, and an unnamed group containing the newer Nipah and Hendra viruses. While gene order among these groups of viruses is similar, Nipah and Hendra viruses have been found to be larger in size primarily due to intragenic noncoding regions. Phylogenetic analysis of the nucleoprotein (N) gene further supports this division into four genera that make up the subfamily Paramyxovirinae: parainfluenza viruses (e.g . Human parainfluenza 1 and 3 viruses), rubulaviruses (e.g. mumps, New Castle disease virus), morbilliviruses (e.g. measles virus, canine distemper virus), and a proposed new genus containing Nipah and Hendra viruses. Respiratory syncytial viruses (RSV) make up the other subfamily.

Paramyxoviruses are responsible for a range of human diseases, from acute pharyngitis and laryngeotracheobronchitis (croup) due to human parainfluenza viruses 1,2, and 3, and acute reactive airway disease and pneumonia due to RSV, to the vaccine-preventable measles and mumps. Other paramyxoviruses cause a variety of animal diseases, such as New Castle Disease, Rinderpest, and respiratory diseases due to animal and parainfluenza and RSV viruses. Hendra and Nipah viruses are unique in that they have a very wide species range and yet may cause different clinical disease patterns among the susceptible species.

Recent identification and description of other viruses causing animal disease include Menangle virus from swine in Australia and Tupaia virus from tree shrews in Thailand. Although other paramyxoviruses have been isolated from assorted species and described in varying detail in the literature, many are not known to be associated with disease but only minimal investigation of most of these viruses has been undertaken.

The epidemiology of paramyxoviruses in humans varies considerably. Measles virus, transmitted by small particle aerosols from person to person, has caused rapid spread of disease in unvaccinated populations. In contrast, large droplet particle transmission by fomite contamination and autoinoculation is characteristic of RSV. Hendra and Nipah viruses are predominantly transmitted to humans from infected horses and pigs, respectively; the exact mode(s) of transmission is currently not known. However, human-to-human transmission has not been documented definitively for either virus.

Attachment 3

Taken from CDC web site, for more information contact:
http://www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4s4.htm

Office of Health and Safety (OHS)

BMBL Section IV

Vertebrate Animal Biosafety Level Criteria

Biosafety Documents
BMBL Table of Contents

If experimental animals are used, institutional management must provide facilities, staff, and established practices that reasonably ensure appropriate levels of environmental quality, safety, and care. Laboratory animal facilities are simply a special type of laboratory. As a general principle, the biosafety level (facilities, practices, and operational requirements) recommended for working with infectious agents in vivo and in vitro are comparable.

However, it is well to remember that the animal room can present some unique problems. In the microbiological laboratory, hazardous conditions are caused by personnel or by the equipment being used. In the animal room, the activities of the animals themselves can present new hazards. Animals may generate aerosols, they may bite and scratch, and they may be infected with a zoonotic disease.

These recommendations presuppose that laboratory animal facilities, operational practices, and quality of animal care meet applicable standards and regulations (e.g., Guide for the Care and Use of Laboratory Animals(1) and Laboratory Animal Welfare Regulations(2)) and that appropriate species have been selected for animal experiments. In addition, the organization should have an occupational health and safety plan The recent publication of the Institute of Medicine, Occupational Health and Safety in the Care of Research Animals,(3) is most helpful in this regard.

Ideally, facilities for laboratory animals used in studies of infectious or noninfectious

disease should be physically separate from other activities such as animal production and quarantine, clinical laboratories, and especially from facilities providing patient care. Traffic flow that will minimize the risk of cross contamination should be considered in the plans. A "clean/dirty hall" layout may be useful to minimize this risk.

The recommendations detailed below describe four combinations of practices, safety equipment, and facilities for experiments with animals infected with agents that cause, or may cause, human infection. These four combinations, designated Animal Biosafety Levels (ABSL) 1-4, provide increasing levels of protection to personnel and to the environment, and are recommended as minimal standards for activities involving infected laboratory animals. The four ABSLs describe animal facilities and practices applicable to work with animals infected with agents assigned to Biosafety Levels 1-4, respectively.

Investigators inexperienced in conducting these types of experiments should seek help in designing their experiments from individuals who are experienced in this special work.

Facility standards and practices for invertebrate vectors and hosts are not specifically addressed in the standards for commonly used laboratory animals. Laboratory Safety for Arboviruses and Certain Other Viruses of Vertebrates,(4) prepared by the Subcommittee on Arbovirus Laboratory Safety (SALS) of the American Committee on Arthropod-Borne Viruses, serves as a useful reference in the design and operation of facilities using arthropods.

Animal Biosafety Level 1 (ABSL-1)

Animal Biosafety Level 1 (ABSL-1) is suitable for work involving well characterized agents that are not known to cause disease in healthy adult humans, and that are of minimal potential hazard to laboratory personnel and the environment.

A. Standard Practices

1. The animal facility director establishes policies, procedures, and protocols for emergency situations. Each project is subject to pre-approval by the Institutional Animal Care and Use Committee (IACUC) and the Institutional Biohazard Committee (IBC). Any special practices are approved at this time.

2. Only those persons required for program or support purposes are authorized to enter the facility. Before entering, persons are advised of the potential biohazards and are instructed on the appropriate safeguards.

3. An appropriate medical surveillance program is in place.

4. A safety manual is prepared or adopted. Personnel are advised of special hazards, and are required to read and

follow instructions on practices and procedures.

5. Eating, drinking, smoking, handling contact lenses, applying cosmetics, and storing food for human use should only be done in designated areas and are not permitted in animal or procedure rooms.

6. All procedures are carefully performed to minimize the creation of aerosols or splatters.

7. Work surfaces are decontaminated after use or after any spill of viable materials.

8. All wastes from the animal room (including animal tissues, carcasses, and contaminated bedding) are transported from the animal room in leak-proof, covered containers for appropriate disposal in compliance with applicable institutional or local requirements. Incineration is recommended.

9. Policies for the safe handling of sharps are instituted.

10. Personnel wash their hands after handling cultures and animals, after removing gloves, and before leaving the animal facility.

11. A biohazard sign must be posted on the entrance to the animal room whenever infectious agents are present. The hazard warning sign identifies the infectious agent(s) in use, lists the name and telephone number of the responsible person(s), and indicates the special requirements for entering the animal room (e.g., the need for immunizations and respirators).

12. An insect and rodent control program is in effect (see Appendix G).

B. Special Practices: None.

C. Safety Equipment (Primary Barriers):

1. The wearing of laboratory coats, gowns, and/or uniforms in the facility is recommended. Laboratory coats remain in the animal room. Gowns and uniforms are not worn outside the facility.

2. Persons having contact with non-human primates should assess their risk of mucous membrane exposure and wear appropriate eye and face protection.(5)

D. Facilities (Secondary Barriers)

1. The animal facility is separated from areas that are open to unrestricted personnel traffic within the building.

2. External facility doors are self-closing and self-locking. Doors to animal rooms open inward, are self-closing, and are kept closed when experimental animals are present. Cubicle room inner doors may open outward or be horizontal or vertical sliding.

3. The animal facility is designed, constructed, and maintained to facilitate cleaning and housekeeping. The interior surfaces (walls, floors, and ceilings) are water resistant.

4. Internal facility appurtenances, such as light fixtures, air ducts, and utility pipes, are arranged to minimize horizontal surface areas.

5. Windows are not recommended. Any windows must be resistant to breakage. Where possible, windows should be sealed. If the animal facility has windows that open, they are fitted with fly screens.

6. If floor drains are provided, the traps are always filled with water and/or an appropriate disinfectant.

7. Ventilation should be provided in accordance with the Guide for Care and Use of Laboratory Animals, latest edition.(6) No recirculation of exhaust air should occur. It is recommended that animal rooms maintain negative pressure compared to adjoining hallways.

8. The facility has a hand washing sink.

9. Cages are washed manually or in a cage washer. The mechanical cage washer should have a final rinse temperature of at least 180F.

10. Illumination is adequate for all activities, avoiding reflections and glare that could impede vision.

Animal Biosafety Level 2 (ABSL-2)

Animal Biosafety Level 2 involves practices for work with those agents associated with human disease. It addresses hazards from ingestion as well as from percutaneous and mucous membrane exposure. ABSL-2 builds upon the practices, procedures, containment equipment, and facility requirements of ABSL-1.

A. Standard Practices

1. Aside from the standard policies, procedures, and protocols for emergency situations established by the facility director, appropriate special policies and procedures should be developed as needed and approved by the Institutional Animal Care and Use Committee (IACUC) and the Institutional Biohazard Committee (IBC).

2. Access to the animal room is limited to the fewest number of individuals possible. Personnel who must enter the room for program or service purposes when work is in progress are advised of the potential hazard.

3. An appropriate medical surveillance program is in place. All personnel receive appropriate immunizations or tests for the agents handled or potentially present (e.g., hepatitis B vaccine, TB skin testing). When appropriate, a serum surveillance system should be implemented.(7)

4. A biosafety manual is prepared or adopted. Personnel are advised of special hazards, and are required to read and follow instructions on practices and procedures.

5. Eating, drinking, smoking, handling contact lenses, applying cosmetics, and storing food for human use should only be done in designated areas and are not permitted in animal or procedure rooms.

6. All procedures are carefully performed to minimize the creation of aerosols or splatters.

7. Equipment and work surfaces in the room are routinely decontaminated with an effective disinfectant after work with the infectious agent, and especially after overt spills, splashes, or other contamination by infectious materials.

8. All infectious samples are collected, labeled, transported, and processed in a manner that contains and prevents transmission of the agent(s). All wastes from the animal room (including animal tissues, carcasses, contaminated bedding, unused feed, sharps, and other refuse) are transported from the animal room in leak-proof, covered containers for appropriate disposal in compliance with applicable institutional or local requirements. The outer surface of the containers is disinfected prior to moving the material. Autoclaving of the contents prior to incineration is recommended.

9. Policies for the safe handling of sharps are instituted:

a. Needles and syringes or other sharp instruments are

restricted for use in the animal facility only when there is no alternative, such as for parenteral injection, blood collection, or aspiration of fluids from laboratory animals and diaphragm bottles.

b. Syringes that re-sheathe the needle, needle-less systems, and other safe devices should be used when appropriate.

c. Plasticware should be substituted for glassware whenever possible.

10. Personnel wash their hands after handling cultures and animals, after removing gloves, and before leaving the animal facility.

11. A biohazard sign must be posted on the entrance to the animal room whenever infectious agents are present. The hazard warning sign identifies the infectious agent(s) in use, lists the name and telephone number of the responsible person(s), and indicates the special requirements (e.g., the need for immunizations and respirators) for entering the animal room.

12. An insect and rodent control program is in effect (see Appendix G).

B. Special Practices

1. Animal care laboratory and support personnel receive appropriate training on the potential hazards associated with the work involved, the necessary precautions to prevent exposures, and the exposure evaluation procedures. Personnel receive annual updates, or additional training as necessary for procedural or policy changes. Records of all training provided are maintained. In general, persons who may be at increased risk of acquiring infection, or for whom infection might be unusually hazardous, are not allowed in the animal facility unless special procedures can eliminate the extra risk.

2. Only animals used for the experiment(s) are allowed in the room.

3. All equipment must be appropriately decontaminated prior to removal from the room.

4. Spills and accidents which result in overt exposures to infectious materials must be immediately reported to the facility director. Medical evaluation, surveillance, and treatment are provided as appropriate and written records are maintained.

C. Safety Equipment (Primary Barriers)

1. Gowns, uniforms, or laboratory coats are worn while in the animal room. The laboratory coat is removed and left in the animal room. Gowns, uniforms, and laboratory coats are

removed before leaving the animal facility. Gloves are worn when handling infected animals and when skin contact with infectious materials is unavoidable.

2. Personal protective equipment is used based on risk assessment determinations (see Section V). Appropriate face/eye and respiratory protection is worn by all personnel entering animal rooms that house nonhuman primates.(8)

3. Biological safety cabinets, other physical containment devices, and/or personal protective equipment (e.g., respirators, face shields) are used whenever conducting procedures with a high potential for creating aerosols. These include necropsy of infected animals, harvesting of tissues or fluids from infected animals or eggs, or intranasal inoculation of animals.

4. When needed, animals are housed in primary biosafety containment equipment appropriate for the animal species. Filter top cages are always handled in properly designed and operating animal biocontainment cabinets recommended for rodents.

D. Facilities (Secondary Barriers)

1. The animal facility is separated from areas that are open to unrestricted personnel traffic within the building.

2. Access to the facility is limited by secure locked doors. External doors are self-closing and self-locking. Doors to animal rooms open inward, are self-closing, and are kept closed when experimental animals are present. Cubicle room inner doors may open outward or be horizontal or vertical sliding.

3. The animal facility is designed, constructed, and maintained to facilitate cleaning and housekeeping. The interior surfaces (walls, floors, and ceilings) are water resistant.

4. Internal facility appurtenances, such as light fixtures, air ducts, and utility pipes, are arranged to minimize horizontal surface areas.

5. Windows are not recommended. Any windows must be resistant to breakage and should be sealed.

6. If floor drains are provided, the traps are always filled with an appropriate disinfectant.

7. Exhaust air is discharged to the outside without being recirculated to other rooms. Ventilation should be provided

in accordance with criteria from Guide for Care and Use of Laboratory Animals, latest edition. The direction of airflow in the animal facility is inward; animal rooms should maintain negative pressure compared to adjoining hallways.

8. Cages are washed manually or in an appropriate cage washer. The mechanical cage washer should have a final rinse temperature of at least 180F.

9. An autoclave is available in the animal facility to decontaminate infectious waste.

10. A hand washing sink is in the animal room where infected animals are housed, as well as elsewhere in the facility.

11. Illumination is adequate for all activities, avoiding reflections and glare that could impede vision.

Animal Biosafety Level 3 (ABSL-3)

Animal Biosafety Level 3 involves practices suitable for work with animals infected with indigenous or exotic agents that present the potential of aerosol transmission and of causing serious or potentially lethal disease. ABSL-3 builds upon the standard practices, procedures, containment equipment, and facility requirements of ABSL-2.

A. Standard Practices

1. Aside from the standard policies, procedures, and protocols for emergency situations established by the facility director, appropriate special policies and procedures should be developed as needed and approved by the Institutional Animal Care and Use Committee (IACUC) and the Institutional Biosafety Committee (IBC).

2. The laboratory or animal facility director limits access to the animal room to the fewest number of individuals possible. Personnel who must enter the room for program or service purposes when work is in progress are advised of the potential hazard.

3. An appropriate medical surveillance program is in place. All personnel receive appropriate immunizations or tests for the agents handled or potentially present (e.g., hepatitis B vaccine, TB skin testing). When appropriate, a serum surveillance system should be implemented.(9) In general, persons who may be at increased risk of acquiring infection, or for whom infection might have serious consequences, are

not allowed in the animal facility unless special procedures can eliminate the extra risk. Assessment should be made by the occupational health physician.

4. A biosafety manual is prepared or adopted. Personnel are advised of special hazards, and are required to read and follow instructions on practices and procedures.

5. Eating, drinking, smoking, handling contact lenses, applying cosmetics, and storing food for human use should be done only in designated areas and are not permitted in animal or procedure rooms.

6. All procedures are carefully performed to minimize the creation of aerosols or splatters.

7. Equipment and work surfaces in the room are routinely decontaminated with an effective disinfectant after work with the infectious agent, and especially after overt spills, splashes, or other contamination by infectious materials.

8. All wastes from the animal room (including animal tissues, carcasses, contaminated bedding, unused feed, sharps, and other refuse animal tissues) are transported from the animal room in leak-proof, covered containers for appropriate disposal in compliance with applicable institutional or local requirements. Incineration is recommended. The outer surface of the containers is disinfected prior to moving the material (see Special Practices #3 below).

9. Policies for the safe handling of sharps are instituted.

a. Needles and syringes or other sharp instruments are restricted in the animal facility for use only when there is no alternative, such as for parenteral injection, blood collection, or aspiration of fluids from laboratory animals and diaphragm bottles.

b. Syringes that re-sheathe the needle, needle-less systems, and other safe devices should be used when appropriate.

c. Plasticware should be substituted for glassware whenever possible.

10. Personnel wash their hands after handling cultures and animals, after removing gloves, and before leaving the animal facility.

11. A biohazard sign must be posted on the entrance to the animal room whenever infectious agents are present. The hazard warning sign identifies the infectious agent(s) in use, lists the name and telephone number of the responsible

person(s), and indicates the special requirements for entering the animal room (e.g., the need for immunizations and respirators).

12. All infectious samples are collected, labeled, transported, and processed in a manner that contains and prevents transmission of the agent(s).

13. Laboratory and support personnel receive appropriate training on the potential hazards associated with the work involved, the necessary precautions to prevent exposures, and the exposure evaluation procedures. As necessary, personnel receive updates and/or additional training on procedural or policy changes. Records of all training provided are maintained.

14. An insect and rodent control program is in effect.

B. Special Practices

1. Cages are autoclaved or thoroughly decontaminated before bedding is removed and before they are cleaned and washed. Equipment must be decontaminated according to any local, state, or federal regulations before being packaged for transport or removal from the facility for repair or maintenance.

2. A spill procedure is developed and posted. Only personnel properly trained and equipped to work with infectious materials are to clean up spills. Spills and accidents that result in overt exposures to infectious materials must be immediately reported to the facility director. Medical evaluation, surveillance, and treatment are provided as appropriate and written records are maintained.

3. All wastes from the animal room must be autoclaved prior to incineration or other appropriate terminal treatment.

4. Materials not related to the experiment (e.g., plants, animals) are not permitted in the animal room.

C. Safety Equipment (Primary Barriers)

1. Uniforms or scrub suits are worn by personnel entering the animal room. Wrap-around or solid-front gowns should be worn over this clothing. Front-button laboratory coats are unsuitable. The gown must be removed and left in the animal room. Before leaving the animal facility, scrub suits and uniforms are removed and appropriately contained and decontaminated prior to laundering or disposal.

2. Personal protective equipment used is based on risk assessment determinations.

a. Personal protective equipment is used for all activities involving manipulations of infectious material or infected animals.

b. Personnel wear gloves when handling infected animals. Gloves are removed aseptically and autoclaved with other animal room wastes before disposal.

c. Appropriate face/eye and respiratory protection (e.g., respirators and face shields) is worn by all personnel entering animal rooms.

d. Boots, shoe covers, or other protective footwear, and disinfectant foot baths are available and used where indicated.

3. The risk of infectious aerosols from infected animals or their bedding also can be reduced if animals are housed in containment caging systems, such as open cages placed in inward flow ventilated enclosures (e.g., laminar flow cabinets), solid wall and bottom cages covered with filter bonnets, or other equivalent primary containment systems.

4. Biological safety cabinets and other physical containment devices are used whenever conducting procedures with a potential for creating aerosols. These include necropsy of infected animals, harvesting of tissues or fluids from infected animals or eggs, or intranasal inoculation of animals. At BSL-3, all work should be done in a primary barrier; otherwise respirators should be worn by personnel in the room.

D. Facilities (Secondary Barriers)

1. The animal facility is separated from areas that are open to unrestricted personnel traffic within the building.

2. Access to the facility is limited by a self-closing and self-locking door. This exterior entry door may be controlled by a key lock, card key, or proximity reader. Entry into the animal room is via a double-door entry which includes a change room and shower(s). An additional double-door access (air-lock) or double-doored autoclave may be provided for movement of supplies and wastes into and out of the facility, respectively. Doors to animal rooms open inward and are self-closing. Doors to cubicles inside an animal room may open outward or slide horizontally or vertically.

3. The animal facility is designed, constructed, and

maintained to facilitate cleaning and housekeeping. The interior surfaces (walls, floors, and ceilings) are water resistant. Penetrations in floors, walls and ceiling surfaces are sealed and openings around ducts and the spaces between doors and frames are capable of being sealed to facilitate decontamination.

4. A hands-free or automatically operated hand washing sink is provided in each animal room near the exit door. The sink trap is filled with an appropriate disinfectant after each use.

5. Internal facility appurtenances, such as light fixtures, air ducts, and utility pipes, are arranged to minimize horizontal surface areas.

6. Any windows must be resistant to breakage. Where possible, windows should be sealed. If the animal facility has windows that open, they are fitted with fly screens.

7. If floor drains are provided, they are always filled with an appropriate disinfectant.

8. Ventilation should be provided in accordance with criteria from the Guide for Care and Use of Laboratory Animals, latest edition. A ducted exhaust air ventilation system is provided. This system creates directional airflow which draws air into the laboratory from "clean" areas and toward "contaminated" areas. The exhaust air is not recirculated to any other area of the building. Filtration and other treatments of the exhaust air may not be required, but should be considered based on site requirements, and specific agent manipulations and use conditions. The exhaust must be dispersed away from occupied areas and air intakes, or the exhaust must be HEPA-filtered. Personnel must verify that the direction of the airflow (into the animal areas) is proper. It is recommended that a visual monitoring device that indicates and confirms directional inward airflow be provided at the animal room entry. Consideration should be given to installing an HVAC control system to prevent sustained positive pressurization of the animal spaces. Audible alarms should be considered to notify personnel of HVAC system failure.

9. HEPA-filtered exhaust air from a Class II biological safety cabinet can be recirculated into the animal room if the cabinet is tested and certified at least annually. When exhaust air from Class II safety cabinets is to be discharged to the outside through the building exhaust air system, the cabinets must be connected in a manner that avoids any interference with the air balance of the cabinets or the building exhaust system (e.g., an air gap between the

cabinet exhaust and the exhaust duct). When Class III biological safety cabinets are used, they should be directly connected to the exhaust system. If the Class III cabinets are connected to the supply system, it is done in a manner that prevents positive pressurization of the cabinets (see Appendix A).

10. Cages are washed in a cage washer. The mechanical cage washer has a final rinse temperature of at least 180F.

11. An autoclave is available which is convenient to the animal rooms where the biohazard is contained. The autoclave is utilized to decontaminate infectious waste before moving it to other areas of the facility.

12. If vacuum service (i.e., central or local) is provided, each service connection should be fitted with liquid disinfectant traps and an in-line HEPA filter, placed as near as practicable to each use point or service cock. Filters are installed to permit in-place decontamination and replacement.

13. Illumination is adequate for all activities, avoiding reflections and glare that could impede vision.

14. The completed Biosafety Level 3 facility design and operational procedures must be documented. The facility must be tested for verification that the design and operational parameters have been met prior to operation. Facilities should be re-verified at least annually against these procedures as modified by operational experience.

15. Additional environmental protection (e.g., personnel showers, HEPA filtration of exhaust air, containment of other piped services, and the provision of effluent decontamination) should be considered if recommended by the agent summary statement, as determined by risk assessment of the site conditions, or other applicable federal, state, or local regulations.

Animal Biosafety Level 4 (ABSL-4)

Animal Biosafety Level 4 involves practices suitable for addressing dangerous or exotic agents that pose high risk of life threatening disease, aerosol transmission, or related agents with unknown risk of transmission. ABSL-4 builds upon the standard practices, procedures, containment equipment, and facility requirements of ABSL-3. Procedures must be developed locally to address specific operations of the Class III cabinet line or the suit laboratory.

A. Standard Practices

1. Aside from the standard policies, procedures, and protocols for emergency situations established by the facility director, appropriate special policies and procedures should be developed as needed and approved by the Institutional Animal Care and Use Committee (IACUC) and the Institutional Biosafety Committee (IBC).

2. The laboratory or animal facility director limits access to the animal room to the fewest individuals possible. Personnel who must enter the room for program or service purposes when work is in progress are advised of the potential hazard.

3. A medical surveillance program must be instituted for all persons entering an ABSL-4 facility. This program must include appropriate immunizations, serum collection, and availability of post-exposure counseling and potential prophylaxis.(10) In general, persons who may be at increased risk of acquiring infection, or for whom infection might have serious consequences, are not allowed in the animal facility unless special procedures can eliminate the extra risk. Assessment should be made by the occupational health physician.

4. A site-specific biosafety manual is prepared or adopted. Personnel are advised of special hazards, and are required to read and to follow instructions on practices and procedures.

5. Eating, drinking, smoking, handling contact lenses, applying cosmetics, and storing food for human use should be done only in designated areas and are not permitted in animal or procedure rooms.

6. All procedures are carefully performed to minimize the creation of aerosols or splatters.

7. Equipment and work surfaces in the room are routinely decontaminated with an appropriate disinfectant after work with the infectious agent, and especially after overt spills, splashes, or other contamination by infectious materials.

8. A spill procedure is developed and posted. Only personnel properly trained and equipped to work with infectious materials are to clean up spills. Spills and accidents that result in overt exposures to infectious materials must be immediately reported to the facility director. Medical evaluation, surveillance, and treatment are provided as appropriate and written records are maintained.

9. All wastes (including animal tissues, carcasses, and contaminated bedding), other materials for disposal, and clothing to be laundered, are sterilized in a double-door autoclave located in the secondary barrier wall of the facility (see B-4 below). Disposable wastes are incinerated.
10. Policies for the safe handling of sharps are instituted.

a. Needles and syringes or other sharp instruments are restricted in the animal facility for use only when there is no alternative, such as for parenteral injection, blood collection, or aspiration of fluids from laboratory animals and diaphragm bottles.

b. Syringes that re-sheathe the needle, needle-less systems, and other safe devices should be used when appropriate.

c. Plasticware should be substituted for glassware whenever possible

11. A biohazard sign must be posted on the entrance to the animal room whenever infectious agents are present. The hazard warning sign identifies the infectious agent(s) in use, lists the name and telephone number of the responsible person(s), and indicates the special requirements for entering the animal room (e.g., the need for immunizations and respirators).

12. Laboratory personnel receive appropriate training on the potential hazards associated with the work involved, the necessary precautions to prevent exposures, and the exposure evaluation procedures. Personnel receive annual updates, or additional training as necessary for procedural or policy changes. Records are maintained on all training provided.

13. Cages are autoclaved or thoroughly decontaminated before bedding is removed and before they are cleaned and washed. Equipment and work surfaces are routinely decontaminated with an appropriate disinfectant after work with infectious materials, and especially after spills, splashes, or other contamination by infectious materials. Equipment must be decontaminated according to any local, state, or federal regulations before removal from the facility for repair or maintenance.

14. Personnel assigned to work with infected animals should work in pairs. Based on the risk assessment (see Section V), use of squeeze cages, working only with anesthetized animals, or other appropriate procedures to reduce possible worker exposure must be instituted.

15. Materials not related to the experiment (e.g., plants, animals) are not permitted in the facility.

B. Special Practices

1. Additional measures are effected to control access (e.g., 24-hour guard and check in/out system). Personnel enter and leave the facility only through the clothing change and shower rooms. Personnel shower each time they leave the facility. Personnel should not enter or leave the facility through the air locks, except in an emergency.

2. In a Class III cabinet operation, personal clothing is removed in the outer clothing change room and kept there. Complete laboratory clothing, including undergarments, pants and shirts or jump suits, shoes, and gloves, is provided and used by personnel entering the facility. When exiting, personnel remove laboratory clothing in the inner change room before entering the shower area. Soiled clothing is sterilized in an autoclave.

3. In an ABSL-4 suit operation, a complete clothing change is required. A personal shower is required following removal of the decontaminated suit. Soiled lab clothing is autoclaved before laundering.

4. Supplies and materials are introduced into the facility via a double-door autoclave or fumigation chamber. After the outer door is secure, personnel inside the facility open the inner door to retrieve the materials. The doors of the autoclave and fumigation chamber are interlocked in a manner that prevents opening of the outer door unless the autoclave has been operated through a "sterilization cycle" or the fumigation chamber has been decontaminated.

5. A system is established for the reporting of accidents, incidents, exposures, and employee absenteeism, and for the medical surveillance of potential laboratory-associated illnesses. An essential adjunct to such a reporting/surveillance system is the availability of a facility for the quarantine, isolation, and medical care of persons with potential or known laboratory-associated illnesses.

6. The serum samples collected are analyzed at intervals. The results are communicated to the participants.

C. Safety Equipment (Primary Barriers)

1. Laboratory animals infected with Biosafety Level 4 agents must be housed within a Class III biological safety cabinet in a BSL-4 Cabinet Laboratory. In a BSL-4 Suit Laboratory, all personnel are required to wear one-piece positive pressure suits ventilated with a life support system.

Infected animals should be housed in a partial containment system (such as open cages placed in ventilated enclosures, solid wall and bottom cages covered with filter bonnets and opened in laminar flow hoods, or other equivalent primary containment systems).

2. The use of disposable material that does not require cleaning, including animal caging, should be considered. Disposable materials must be autoclaved on exit from the facility and then incinerated.

D. Facilities (Secondary Barriers)

BSL-4 animal areas may be included as an integral part of BSL-4 Cabinet Laboratories or Suit Laboratories as described in Section III of this document. The facility requirements described in the BSL-4 Laboratory section should be utilized in conjunction with the caging described in the equipment section above.

References

1. Guide for the Care and Use of Laboratory Animals, National Academy Press, Washington, DC, 1996

2. U.S. Department of Agriculture. Laboratory Animal Welfare Regulations - 9 CFR, Subchapter A, Parts 1, 2, and 3.

3. Occupational Health and Safety in the Care of Research Animals. National Academy Press, Washington, D.C., 1996.

4. Subcommittee on Arbovirus Laboratory Safety for Arboviruses and Certain Other Viruses of Vertebrates. 1980. Am J Trop Med Hyg 29(6):1359-1381.

5. Centers for Disease Control and Prevention. 1998. Fatal Cercopithecine herpesvirus 1 (B Virus) Infection Following a Mucocutaneous Exposure and Interim Recommendations for Worker Protection. MMWR 47(49); 1073-6,1083

6. Guide for the Care and Use of Laboratory Animals (1)

7. Occupational Health and Safety in the Care of Research Animals (3)

8. Centers for Disease Control and Prevention. 1998. (5)

9. Occupational Health and Safety in the Care of Research Animals (3)

10. Occupational Health and Safety in the Care of Research Animals. (3)

Attachment 4

Human Case Definition:

History of subjective fever or temperature 37.5° C or headache and evidence of altered mental status (drowsiness, lethargy, confusion, abnormal behavior, irritability or agitation) with or without seizures or focal neurological findings.

Epidemiology

Gender	n	(%)	Occupation	n	(%)
Male	230	**(82)**	**Pig farmer**	2 2 1	**(78)**
			Lorry driver	7	**(2.5)**
Ethnicity			**Abattoir worker**	4	**(1.4)**
Chinese	198	**(70)**	**Pig culler**	4	**(1.4)**
Indian	48	**(17)**	**No pig contact**	8	**(3)**
Malay	7	**(2.5)**			
Nepalese	7	**(2.5)**			

Histopathological Findings:

Vasculitis: syncytitial cells, cytolysis, necrosis
Cerebral cortex, brainstem, lungs, kidneys

Immunohistochemical staining for viral antigen
Endothelial cells of the CNS
Kidney tubules
Lung

Attachment 5

Preliminary Case Definition for Pigs:

Weaners (> 4 weeks) and growers : Acute febrile (39.9° C) illness with respiratory signs ranging from increased or forced respiration to harsh nonproductive cough or open mouth breathing which may be accompanied by one or more of the following neurological signs:

Trembles/neuralgic twitches/muscle fasciculation/tetanic spasms
Rear leg weakness

Sows: Acute febrile (39.9° C) illness with labored breathing (open mouth), increased salivation, nasal discharge (possibly bloody) and possible abortion (1st trimester). Sows and boars may die very rapidly (within 24 hours) with no signs of clinical disease. Some or all of the following neuralgic signs may be present:

Head pressing
Agitation/biting at bars
Tetanic spasms

Disease has been identified in suckling pigs at this time and seems to have the highest mortality in this group
Sows may have a bloody nasal discharge and head bruising at death
Boars and sows are similar in disease presentation

Attachment 6

Necropsy on a 6-8 week old Yorkshire (cross) castrated pig

Temperature 104.5, Pulse 125, Respiration 90, very hoarse non-productive cough
Auscultation: moist rales
20 lb. pig without any external signs of disease, other than being a little gaunt, respiration increased and cough

Postmortem: Excessive pericardial fluid, the fluid is straw colored. The lungs are moist and edematous, with sharp lines of demarcation in the ventral aspects of the apical lobes. Petechial and ecchymotic hemorrhages are present.

Tissues submitted:
Lung, cardiac, liver, kidney, brain, lymph nodes, spleen, pericardial fluid, blood

Necropsy on a 3-year-old sow
Temperature 102.4, Pulse 130, Respiration 80
Auscultation: nothing noted

Clinically the sow was having continuous seizures and foaming from the mouth. She was in her 3rd trimister of pregnancy. She was in good flesh. The owner indicated that she had been fine the day before.

Postmortem exam revealed that the lung and the brain were the only two tissues that exhibited gross pathologic changes. The lungs are moist and edematous, with sharp lines of demarcation in the ventral aspects of the apical lobes. Petechial and ecchymotic hemorrhages are present. The brain of the sow exhibited vascular congestion and petechial hemorrhages.

All animals that were posted exhibited similar findings.

Attachment 7

CASE DEFINITION FOR PIGS
Week 2

Weaners (>4 weeks) and growers: Acute febrile (>39.9 C) illness with respiratory signs ranging from increased or forced respiration to harsh loud non-productive cough or open mouth breathing, epistaxis, accompanied by one or more of the following neurological signs:
Trembles/neuralgic twitches/muscle fasciculation/ tetanic spasms and incoordination
Rear leg weakness and varying degrees of paresis

Sows: Acute febrile (>39.9 C) illness with labored breathing (open mouth), increased salivation, nasal discharge (possibly bloody) and possible abortion (1st trimester). Sows and boars may die very rapidly (24 hours) with no signs of clinical disease. Some or all of the following neuralgic signs may be present:

Head pressing
Agitation/biting at bars
Tetanic spasms

Sows may have a bloody nasal discharge at death.
Boars and sows are similar in disease presentation.

Necropsy Findings - Gross pathology

Emphysematous lungs with fresh hemorrhages in interlobular septa and petechial hemorrhages on lungs. In acute case, agonal hemorrhages are observed with clear distinct borders. The bronchi and trachea may be filled with frothy fluid with or without blood. Varying levels of tracheal epithelium congestion is observed.
Cerebral and cerebellar congestion and hemorrhage

Histopathology

Vasculitis: syncytitial cells, cytolysis, necrosis
Cerebral cortex, brainstem, lungs, kidneys

Immunohistochemical staining for viral antigen
Endothelial cells of the CNS
Kidney tubules
Lungs, Immunohistochemical staining is more evident in the lungs of pig compared to humans

Attachment 8

Hendra virus IgG and IgM Testing for Hendra-like virus in State A

The test results that we are releasing on patients are those performed using virus antigens and reagents prepared to the prototype strain of Hendra virus. Our laboratory determined that the virus isolated from encephalitis patients is 10-12 percent different from Hendra virus nucleotide sequence. Comparative serology has not yet been performed with reagents prepared with the new State A virus and such results will be forthcoming in the coming weeks. Until then, the tests for Hendra virus antibodies will have to suffice.

We are reporting the results of an IgM capture ELISA for Hendra virus and an indirect IgG ELISA also performed with Hendra virus antigens. The results are reported as "Pos" for reactive or positive tests, "Neg" for non-reactive or negative results, and "+/-" for results which are at the marginal area between positive and negative results. Sera are tested at a beginning dilution of 1:100 and CSF at a beginning dilution of 1:20 .

The assay was optimized utilizing the serum of a person who survived Hendra virus infection in Australia. The practical clinical experience with the assays is limited to that which we've been able to gain in this outbreak. We are attempting to conservatively interpret the results of the assays and need to gain from our experience as we progress in testing through the outbreak. In other words, we are not reporting positive results unless the values are significant. Any questionable results are being reported as "+/-" and should not be interpreted beyond indicating that an additional sample taken at a later date may clarify the ultimate diagnosis in the patient.

The IgM capture assay, as in other diagnostic situations for acute viral encephalitis, appears to offer the earliest indication of infection with the new Hendra-like virus. In the limited number of tests that we have so far performed, the serum is often positive for IgM capture antibody before the CSF becomes positive. Most of the specimens that we have are from acute specimens taken from patients in the early stages of their disease; it appears that as might be expected in this situation, there are many samples that have IgM with no IgG. In the few patients from whom we have serial samples taken over a period of a week or more, IgG does appear in the later samples of both the serum and the cerebrospinal fluid.

As we progress through the outbreak and as additional tests become available, we may issue further updates on some of these patients. Until then, please accept these laboratory results as tentative but accept them as the best we can do until we have additional reagents and more information available.

Test results for pigs dogs and cats use the same method and continue to be processed daily.

Disease Outbreak

Don Noah, DVM, MPH
Mike Peterson, DVM, MPH, DrPH

SCENARIO
Season: Fall
Position: Veterinary Officer in a federal/state organization
Location: Midwestern U.S.

- A colleague at a nearby college of veterinary medicine mentions to you over a beer that during recent ambulatory calls she has seen what she describes as a higher than normal morbidity rate of respiratory disease among horses (the disease resolves with supportive therapy)
- A week later, over another beer, a second veterinary colleague in companion animal practice mentions to you that he is seeing what he describes as a new URI in cats with CNS sequelae and 100% mortality in spite of intense supportive therapy
- While listening to NPR while sipping a beer at home, you hear reports of a flu-like illness among the general public in the Midwest with what appears to be a higher than usual mortality rate among all age groups

Questions
- Do you have enough information to consider that there may be a connection among these events?
- If not, what other information would you need to consider these events to be related?
- If so, what are your next actions?

Describing the Outbreak/Questions
- You have decided the events are related or potentially related.
- What do you do next to confirm the presence of an outbreak?
- Whom do you contact?
- What additional steps need to be taken to confirm an animal outbreak?

Response
- The presence of an outbreak among three species caused by a new agent has been scientifically established.
- There have been no further reports in the media other than the flu-like illness among humans (i.e., no media reports of animal disease).
- Discuss the pros and cons of notifying the media of a potential link among the sick horses, cats and humans
- Defend your decision regarding media notification, detailing steps to be taken.

Scenario Continues/Questions

- Efforts to describe the disease in all species are ongoing. However, early interventions have not stopped the spread of disease in any species affected.
- What do you see as the responsibilities/interactions among federal/state/practicing DVMs and the public health community?
- What do you see as your role in reassuring the public at large, pet owners and horse enthusiasts?
- What risk communication efforts should you undertake?

After-action steps (Scenario I)

- The disease has waned from epidemic levels in all three species.
- You are being asked questions related to emerging infections. How do you reassure your constituency in general terms?

After-action steps (Scenario II)

- The disease continues to rage in all three species with horses having been identified as a reservoir and an amplifying host.
- What additional actions do you recommend?
- What do you see as your organization's role in this outbreak?

The End

- Congratulations! Have a beer - you saved the country from disease x!

A New Virus in Malaysia

T. G. Ksiazek, D.V.M., Ph.D.
Special Pathogens Branch
Division of Viral and Rickettsial Diseases
National Center for Infectious Diseases
Centers for Disease Control

A new virus in Malaysia
Malaysian Component

- Ministry of Health, Communicable Disease Control
- Department of Veterinary Services
  - Veterinary Research Institute
- Institute of Medical Research
- University of Malaya

International Component

- **Centers for Disease Control**
  - Special Pathogens Branch
  - Infectious Disease Pathology Activity
  - Respiratory and Enteric Viruses Branch
  - Division of Vector-borne Infectious Diseases
- **Australian Animal Health Laboratory, CSIRO**
- **Department of Primary Industries, Queensland**

Hendra virus

- **Three episodes in Australia**
  - **All involving horses, 2 involving man**
    - 1994 Mackay Australia
    - 1994 Brisbane (Hendra)
    - 1999 Cairns

Special Pathogens
Hendra Connection

- **Biosecurity review and recommendations: BSL-4**
- **Geelong Lab has BSL-4 capability in initial construction, never utilized**
- **Operational BSL-4 consultation for Hendra Operations DEC 1995**
- **Virus Strain passed to CDC**
- **Basic Diagnostic Reagent Set Made:**
  - IgG ELISA
  - IgM ELISA
  - Rabbit and Mouse hyperimmune antibodies: IHC

Australian Ecological Investigations (1)

- **Initially, broad-based search**
  - No antibody in horses, save in survivors at Hendra, in extensive testing of many thousand animals
  - No antibody in other animal species caught surrounding initial outbreak (dogs, cats, etc)

Australian Ecological Investigations (2)

- By chance, a virus isolated from bats that had been "rescued". Virus identified as Hendra Serology of various species indicates that *Pteropus* spp. bats have moderate prevalence of Hendra virus antibodies.

Additional Virus Ecology

- Serology on bats from Papua New Guinea indicates *Pteropus* spp. also have moderate prevalence for Hendra virus
- Malaysia
  - Stay tuned ….

Viral Encephalitis Outbreak in Malaysia

- **Outbreak of Viral Encephalitis in Malaysia:**
  - Disease in Humans with cases described as beginning in October 1998
  - Parallel disease in pigs, but not initially reported nor well described Japanese encephalitis diagnosed as the etiology of the disease in humans *and pigs*

Viral Encephalitis in Malaysia

- Technical information passed to public health policy makers included many of the initial patients with laboratory diagnosis of JE
  - Antibody
  - RT-PCR on CSF (and serum)
  - "Mutant" strain of JE

Map of Malaysia

Outbreak Areas

Map of Southern Outbreak Focus

Eureka

- Dr. K.B. Chua innoculates TC with CSF from patients from Negeri Sembelan: yields cytopathic agent
- Dr. K.B.Chua, sera, CSF and virus isolates to CDC DVBID lab in Fort Collins Colorado (16Mar)
- No go with arbovirus typing fluids or PCR primers for wide array of arboviruses
- Cytopathology is distinctly syncytial
- EM--Paramyxovirus like morphology on thin section

Eureka2

- Materials (17Mar) and Dr. Chua to Atlanta (18Mar)

- Spot slide of fixed infected cells is positive with Hendra hyperimmune ascitic fluids with appropriate controls by IFAT
- 12/13 Patients positive by Hendra IgM capture vs 1/13 JE IgM capture
- RT-PCR is positive with degenerate paramyxovirus P-protein primers, sequence is Hendra-like but distinct (20Mar)

Setting Up Field Investigation
- Speak with State Desk Officer and then DCM Malaysia
- Contact with MOH via Embassy and via Dept Med Micro, Faculty of Medicine, UM
- Invitation on 19Mar
- Depart of 20Mar

Epidemiologic Findings (N=282)
Distribution of Viral Encephalitis Cases (Gender) as of 26May99
Case-Patient Age Distribution as of 26May99
Case Patient Occupation in Kinta and Negeri Sembilan as of 26May99
Racial Distribution of Case-Patients

Methods - Clinical Investigation
- **Examined patients at 6 major hospitals**
  - Ipoh (3), Seremban (1), Kuala Lumpur (2)
- **Set up national encephalitis clinical registry**
  - Developed uniform chart abstraction form
  - Abstracted data from hospital records
  - Distributed forms to physicians to complete

Disease in Humans
- Febrile Illness -4-7 days duration
- Early respiratory signs?
- Headache, drowsiness, slurred speech, loss of cognition, coma
- Neurological signs suggest mid-brain, pons
- Pathology: diffuse focal lesions of CNS
- Mortality ~35%of those hospitalized

Other Diagnostic Findings
- CT scan-brain (n=38)
  - 10 (26%)
    - 5 - cerebral edema
    - 5 - infarction
- MRI-brain (n=2)
  - 2- multiple small T2 signal changes
- EEG (n=6)
  - 6- diffuse slow waves with epileptiform discharges

Diffuse Focal CNS Lesions
Diffuse Focal CNS Lesions, IHC

Vasculitis, Syncitia, IHC
Neuronal Infection, IHC
Neuronal Infection, IHC

Disease in Pigs
- Febrile respiratory disease predominates
  - Labored or forced breathing
  - "One-Mile" cough
- CNS disease much rarer than in man
- Sudden death/neurological disease in sows and boars, some abortions reported
- Mortality 1-3%
- Post-mortem primarily in lung, some CNS

Swine Disease
Swine Nervous Disease
Collection
Post Mortem
Respiratory Involvement
Nervous Involvement
Pig Lung
Pig Lung, IHC
Pig Lung, IHC
Pig Kidney, IHC
Other Species
Dog Lung
Dog Kidney, IHC
Dog Spleen, IHC
Dog Heart, IHC
Dog Assessment

Control
- Immediately stop contact with infected pigs
- Destroy infected pigs in epidemic areas with appropriate personal protection
- Find other infected herds
  - Lab testing Set up in Veterinary Research Institute, Ipoh
  - Initiation of National Swine Surveillance Program

Culling
JE-Hendra Case-Patient Date Onset
National Swine Surveillance
- Limited Period (90 days)
- All premises sampled
  - Based on high morbidity data from invest.
  - 15 sows

    - 2 samples (at least 21 days apart)
- Supplemental abattoir sampling
- Active disease discovery
- Human case discovery
- Cull infected premises

Results of Phase II Nat. Swine Surveillance
Other Investigations
- **Risk Factors:**
    - Direct Pig Contact
- **Virus molecular epidemiology**
    - Pigs--Cases
- **Nosocomial Infections?**
    - No
- **Natural reservoir?**
    - Searching
- **Other Species:**
    - Dogs, Cats, Horses: but not spreading
    - Rodents, birds, insectivores: no or very low

Epidemiology/Epizootiology
- **Human cases:**
    - Direct contact
    - No human to human transmission evident
- **Spread**
    - Movement of infected animals
- **Transmission in Swine:**
    - Very Transmissible in modern husbandry setting: Crowding
- **Virus Maintenance in Swine?**
    - Continuous transmission?
    - Persistent infections?

Molecular Epidemiology
All isolates identical in small p-gene and matrix sequence Initial Human Isolate (Mar 99)
- Earliest Human tissue, Ipoh, Oct 98
- Pig tissues on "hot" farm Mar 98
- Isolate from Singapore Human Case
- Dog Isolate from N. Sembilan

Summary of Mol. Biol.
- Virus segregates in lineage with Hendra
- Nipah and Hendra likely to be members of a new genus within subfamily Paramyxovirinae

- Homology of proteins with Hendra in the range of 67-92% (AA), NC and M proteins
- Greatest homology with other members of subfamily is 46%

Reservoir?

- Total of ~310 bats

Moderate antibody prevalence found in 2 species of *Pteropus*: *Pteropus vampyrus* and *P. hypomalenus*

Virus isolation attempts are pending

Outbreak Summary

- First laboratory confirmed human cases Jan 1997
- Swine disease is rumored to have been present as well--materials for testing?
- Disease experimentally reproduced at Geelong
  - Swine and cats
  - Readily transmissable among swine
- Molecular evidence supports single chain of transmission

Preliminary evidence points to *Pteropus spp.*

New Virus, Unique Situation

- Zoonotic Virus in domestic livestock with high mortality for infected humans
- Control is paramount
  - Cooperation between veterinary and public health authorities necessary
- Eradication of the disease is necessary for the industry to regain the confidence of the consumer

Control Efforts Continue

- Culling of infected herds--Immediate in affected outbreak area (Phase I)
- Discovery and Culling of other infected premises (Phase II)
- Last Human Cases, Late May 1999
- Politics

Outlook?

Killing Animals is Killing Animals

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Introduction

When talking about animal slaughter we use euphemisms like dispatch, euthanasia, put to sleep, but they all mean the same thing; killing animals is killing animals. I understand that there is a big difference between my experience slaughtering cattle and the experiences some veterinarians are faced with when called upon to kill large numbers of animals during disease outbreaks, but whether killing animals in the controlled environment of a slaughter plant or an on-site location for disease eradication, the psychological hazards remain the same. The symptoms I experienced as a result of my exposure to animal slaughter point to an acute stress disorder that could have developed into full blown a post traumatic stress disorder if I would not have received the caring support from colleagues and friends. Veterinarians can also experience the same or similar stress disorders when exposed to killing large numbers of animals. This paper calls for an increased implementation of scientific and technical knowledge when handling large numbers of animals for disease eradication in order to prepare veterinarians for the psychological hazards, understand and recognize acute stress disorders, and most importantly, prevent post traumatic stress disorders.

Personal Experience

Several years ago I was asked to participate in a research project at a large commercial slaughter plant. I had never been in a slaughter plant before and had absolutely no experience killing animals. When our crew got to the plant, I was

completely unprepared, both psychologically and intellectually for what I was about to see. The first thing to assault my senses was the smell: a mixture of urine, feces, blood, rendering, sweat, and stress. The heat and the smell from the cattle hovered above the chutes like a toxic cloud. Next was the deafening noise of the plant machinery and the roar of hundreds of cattle hooves on concrete. After making our way through the yards and onto the kill floor, what I saw almost made me gag. Cattle came up the chute into the restrainer and were shot at the rate of four animals every minute. From the restrainer the animals were shackled and hoisted to the rail. Although the animals were dead, their reflex kicking was unnerving because the cattle's hooves hit the bottom of the catwalk mounted above the rail, producing a sound as loud as a shotgun blast. It seemed as if the cattle were venting their rage at being killed. Just the sheer numbers of animals going through the process was overwhelming. I knew that a high speed slaughter plant kills 250 animals an hour for sixteen hours a day, but I was unprepared in seeing this statistic in its bloody reality. That's 4000 cattle a day, fifty-two weeks a year. Knowing that there are 22 plants the same size and many, many more smaller plants, the numbers become daunting. Just the thought of how many cattle are slaughtered in that one plant is mind boggling. It's a high speed, noisy, smelly, terrifying environment to be in even if you are familiar with it. For somebody like me who had never seen what actually went on, it was a real shock. For several days I had to stand up on the restrainer where the animals were killed and assist the stunner operator. At the end of every day, I was covered from head to toe with brain splatter, blood, and slobber.

Slide #1 Proper position of captive bolt stunner (drawing) Grandin, 1997

Slide #2 Photo of cow in restrainer

We were conducting a brain study that involved collecting a large sample of cattle heads with the brains mostly intact. To do this, I had to develop an alternative method of humanely killing the cattle without destroying the brain. Using a captive bolt stunner, I learned that I could place the stunner behind the poll and aim my shot at the brainstem; this way I could insure instant death and protect the rest of the brain. In order to get a good shot I had to take the time to try and calm the animal, so I was personally getting to know each and every one of the animals for the last minute or two of their lives. That was the hard part.

Although I was overwhelmed by the whole experience, I think I handled the job well. I had so many things on which to concentrate that I must have blocked out the strong emotions that were welling up inside me. However, a few days after the study was over those emotions came spilling out.

Slide # 3: I felt afraid, I had bad dreams, I felt sad

I had a serious case of butterflies in my stomach. I was on edge. I couldn't concentrate on anything. I felt like an unseen predator was stalking me. I had bad dreams. In one dream, a "spirit bull" was chasing me. He was like the spirit of all the cattle in the world that had come and gone, and he was after me because I had done something bad. In one dream I tried to shoot him but the bullets bounced off his head. For several nights I had this horrible dream. I also had recurring dreams of the slaughter plant itself. During the day when I was not being chased by the spirit bull in my dream, I was fighting back the fear that our sample would not be sufficient and we'd have to go back to the plant. Along with that was an overpowering feeling of sadness. The dreams, fear, and sadness

went on for about a week until Temple finally recognized the signs that there was something wrong with me. She started calling me on the phone every two or three hours, and would come over to my house asking me why I felt so bad. I didn't want to talk to anyone, I just wanted to be left alone in my misery.

Slide #4: Logic comes to the rescue

Through persistence and patience, Temple made me talk about my feelings and explain what was specifically bothering me. I told her that I thought I had done something morally wrong and that a higher power was punishing me. Gently, she explained that the emotion circuits in my brain had short-circuited, logic had gone flying out the window, and I was suffering from an acute stress reaction. By providing me with logical, alternative explanations for my irrational fears, day by day I began to calm down and feel better. For example, the way the cattle struggled in the restrainer made me think they had an awareness that they were being slaughtered and they were viewing me as their executioner. She reminded me that I had seen cattle get fearful and excited in exactly the same manner in feed yards and the University Research Station when restrained for vaccinations. When I stopped to think about it, I realized that I had seen cattle struggle worse in feed yards and at the University Research Station than they did at the slaughter plant. The fear I saw in them was not a result of their awareness of death, but of me standing deep in their flight zone. I knew this principle well, but my runaway emotions didn't allow me to make this simple comparison. When I had first walked into the slaughter plant, all of my knowledge about animal behavior was gone because I was unprepared to deal with them in that environment. When I started to understand that the animals were not reacting to me directly or holding me personally responsible, logic

calmed my emotions. Temple emphasized that if we raise cattle with the sense that we are responsible for giving them good lives and assuring that they have painless and fearless deaths, then slaughter is morally sound.

Ever since this experience, I have been interested in the psychiatric literature on acute and post traumatic stress disorders. A big part of the consulting work I do for Temple involves recognizing and reducing stress in cattle during handling. We both follow the psychiatric literature and often talk about the results and findings of new research on stress. In the next section I will discuss both the acute stress reaction I experienced and some of the factors that put me at risk.

Slide # 5 Occupational stress in emergency missions can induce an acute or post traumatic stress disorder… Mitchell, et al 1993 International Handbook of Traumatic Stress Syndromes, Plenum, New York 305-314

Slide # 6: Traumatic stress can be caused by exposure to severely mutilated bodies, the impact of life-threatening events, physically demanding activities, and great material destruction. In many cases, these experiences produce psychological and physiological stress reactions which may lead to physical complaints, mental disorders, and substance abuse…Wagner, et al 1998 Am J Psychiatry 15:1727-1732

I think that veterinarians who are required to kill large numbers of animals during disease outbreaks can be added to the long list of emergency response personnel who are at risk of acute and post traumatic stress disorders. When I began to understand this

literature, I realized that the acute reaction I suffered may have escalated into full blown post traumatic stress if Temple had not intervened when she did and provided the support and hours of talk I needed to reduce the stress and calm my fears. Coworkers, family members, and friends of veterinarians who are exposed to animal slaughter need to be aware of some of the symptoms that are signs of stress disorders so that they may intervene and prevent long term stress conditions which severely affect veterinarians' jobs and their personal lives. There is also the possibility that veterinarians could be prescreened so that those who are at high risk for stress disorders can completely avoid those situations and those who are equipped to deal with animal slaughter are selected. These are the symptoms of acute or post traumatic stress disorders that people should be aware of.

Slide # 7: Symptoms of acute or post traumatic stress disorders

1. **Re-experiencing the event**

   Avoidance of trauma related stimuli

   Increased emotional arousal

   Wagner, et al 1998 Am J Psychiatry 15: 1727-1732

The literature defines an acute stress response as one that lasts less than 30 days, but if it goes past 30 days then it can be diagnosed as post traumatic stress disorder.

The first symptom explains the bad dreams I was having, the second explains the fear of having to go back for a larger sample, and the third explains the sadness. I chose to work with animals because I love animals. I always tried to make their lives better, so

killing them was more than I was equipped to deal with at the time of my exposure to the commercial slaughter plant. I still avoid this trauma related stimuli; Temple makes a point to keep me out of slaughter plants unless my assistance is absolutely required. Constitutionally, she is much better equipped to deal with it. This is part of what keeps her motivated in her mission to improve animal handling around the world. From her work in the slaughter industry, some information she passes on can provide some insights into why some people can adapt to killing large numbers of animals and some cannot.

Slide # 8:Considerable evidence points to the heritability of complex psychological traits that may themselves serve as risk factors for psychiatric disorders.

Kendler 1997 Am J Psychiatry 154:1398-1404

Slide # 9: There are three categories of worker psychology in slaughter plants:

1) **box staplers**
2) **religious ritualists**
3) **sadists**

Slide # 10: The box staplers make up about 70% of the long term stunner operators. They are calm and professional, are not emotionally involved with the animals, are not psychologically stressed, and usually do their jobs well unless they are physically overworked.

Slide # 11: The second category is the sadists. They can be further divided into those who enjoy hurting animals, which is evidenced by laughter, and those who abuse animals because they are afraid and do not know how to handle them properly.

The second sub type of sadism is fairly common. This type of reaction is a defense reaction; they are forced to perform a job that terrifies them, so their reactions are fear-based. Some slaughter plant employees start out killing animals and are just as psychologically and intellectually unprepared as I was. Management needs to be aware of these categories and more selective in hiring those who do the killing. For example, I observed one of the employees at the plant where I was working at during the study who was ill equipped for the job of stunner operator. First of all, he was small and too short to reach over the restrainer and handle heavy equipment, so he was physically stressed. Secondly, he was also extremely jumpy and I could tell that he was afraid of the animals. He was jumping back, terrified, and when the cattle would throw their heads or almost come out of the restrainer, he would overreact and jump on them, hitting them hard a number of times with a cruel intent. Even when they were calm, his defensive reaction was to shoot their eyes out. I did not want to say anything when I was there because I did not want to cause a stir, so I had to sit and watch this. Temple and I talked a lot about this type of person.

1

Slide # 12: Religious Ritual—Examples are rabbis in kosher slaughter plants. His behavior is controlled by a higher power.

Temple taught me to approach the killing of animals as a religious ritualist. This third category can help people deal emotionally with the slaughter of animals. An example of the religious ritualist is a rabbi who performs kosher slaughters. They approach their jobs differently because they believe they are being watched over by a higher being. There are also a number of people in the slaughter industry who take a respectful, religious approach to killing large numbers of animals. Taking this approach to killing involves a belief that there is a higher being taking your actions into account, and you should not abuse the power you have over the animals that have been provided for your use. Being a religious ritualist means taking responsibility as a caregiver, and showing a kind of reverence for the animals.

Without being prepared psychologically or intellectually to kill large numbers of animals during emergency disease control, veterinarians may be at high risk of suffering from acute or post traumatic stress disorders. Temple and I would like to make some recommendations that may prevent this from happening.

Slide # 13: Recommendations for situations where large numbers of animals must be slaughtered

If possible, do it in a commercial slaughter plant. The plant may need to be dedicated solely for the purpose of disease eradication until the outbreak is controlled. Grandin 1998 Emergency Preparedness Meeting Denver, Co.

There are transport considerations and other factors that may make this option unlikely, but every attempt should be made to get the animals to a slaughter plant if the risk for contagion is low.

Slide # 14: The worst thing from a psychological standpoint is shooting animals in a big hole in the ground. If a commercial facility cannot be used then set up a portable chute system and the animals are killed using either electrocution or captive bolt stunners which are methods used in commercial slaughter plants.

From a psychological standpoint, the worst method for killing large numbers of animals is driving them into a pit and then shooting them.

Slide #15: We feel that the psychological well-being of those who must slaughter animals must be protected, so if a commercial facility cannot be utilized, then a portable chute system could be set up, and the animals could be killed using commercial methods, such as electrocution system or a captive bolt stunner. For pigs, a portable trailer mounted electrocution is available from Stork in Holland for mass euthanasia for disease control. For cattle and sheep, a commercially available conveyor restrainer can be set up with portable chutes.

I would like to see this kind of system for cattle, sheep, or pigs, sitting on a flatbed trailer owned by the USDA, parked somewhere locally, within two days of any location. We could also contract slaughter plant employees with experience in killing animals to come out to the location during the strain.

Slide # 16: If we are to maintain humane standards in the animal industry, there must be a manager who is sufficiently involved in the day to day processes of

handling or slaughtering animals, but not so involved that he or she is numb or desensitized.

I would like to discuss further how this can apply to veterinarians. The managers in USDA who send people out to do these slaughter jobs need to take the responsibility to protect the mental health of their employees. Psychological testing is controversial, but I do understand that USDA is attempting to put forth a policy that assures veterinarians can refuse to perform slaughter duties based on moral grounds. Moral grounds are too vague, so I would rather see a policy in place that allows veterinarians to refuse to perform certain duties based on psychological grounds. Because many people in the animal industry are not equipped to deal with slaughter, a veterinarian should have the option and right to refuse; they should be given the benefit of the doubt without a negative impact on their profession. Those veterinarians who feel the need should have independent psychological screenings to determine if they are in a high risk category for stress disorders. The managers who send veterinarians out into the field to perform mass destruction of disease and disease exposed animals need to start considering the risk for psychological stress. The military has done a lot to understand and treat post traumatic stress disorders in Vietnam veterans, and USDA/APHIS could also take the same approach with regard to veterinarians who experience stress disorders as a result of their exposure to the killing of large numbers of animals.